PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P210823PCT1	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/NL2004/000911	International filing date *(day/month/year)* 24.12.2004	Priority date *(day/month/year)* 24.12.2003
International Patent Classification (IPC) or national classification and IPC INV. C12N7/04 C07K14/135 A61K35/76 A61K39/155		
Applicant DE STAAT DER NEDERLANDEN, VERTEGENWOORDIG... et al		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed. as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
28.06.2005	08.06.2006
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Donath, C Telephone No. +49 89 2399-8710

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/NL2004/000911

Box No. I Basis of the report

1. With regard to the **language**, this report is based on

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of:

   ☐ international search (under Rules 12.3(a) and 23.1(b))
   ☐ publication of the international application (under Rule 12.4(a))
   ☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-36 as originally filed

Sequence listings part of the description, Pages

1-19 as originally filed

Claims, Numbers

1-19 as originally filed

Drawings, Sheets

1/5-5/5 as originally filed

☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:

   ☐ the description, pages
   ☐ the claims, Nos.
   ☐ the drawings, sheets/figs
   ☐ the sequence listing *(specify)*:
   ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

   ☐ the description, pages
   ☐ the claims, Nos.
   ☐ the drawings, sheets/figs
   ☐ the sequence listing *(specify)*:
   ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/NL2004/000911

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	17,19
	No:	Claims	1-16,18
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-19
Industrial applicability (IA)	Yes:	Claims	1-19
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

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Supplemental Box relating to Sequence Listing

Continuation of Box I, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ on paper

   ☒ in electronic form

   c. time of filing/furnishing:

   ☒ contained in the international application as filed

   ☐ filed together with the international application in electronic form

   ☐ furnished subsequently to this Authority for the purposes of search and/or examination

   ☐ received by this Authority as an amendment* on

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

* *If item 4 in Box No. I applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded."*

Ad section V.:

1. The following documents are cited:

D1 WO-A-03/029416
D2 Virology **289**, 283-296, 2001
D3 J.Virology **75**, 6825-6834, 2001
D4 Proc.Natl.Acad.Sci.USA **94**, 13961-13966, 1997

2. The present international application refers to pneumoviral virions, such as virions of Respiratory Syncytial Virus, comprising a viral genome that has a mutation in a gene coding for a protein that is essential for infectivity of the pneumovirus, whereby the mutation causes a virus produced from only the viral genome to lack infectivity, and whereby the virion comprises the protein in a form and in an amount that is required for infectivity of the virion. Furthermore, the international application concerns a method for producing said pneumoviral virions, a composition comprising said virion, the use of said virion for the manufacture of a medicament, and a method for the prevention or treatment of a pneumoviral infection by the use of said composition comprising a virion.
In view of the documents cited in the International Search Report only the subject-matter of claims 17 and 19 of the present International application has to be regarded as being new (Article 33(2) PCT).

2.1 D1 describes recombinant respiratory syncytial viruses (RSV) in which all of the surface glycoprotein genes encoding the attachment protein G, the fusion protein F, and the Small Hydrophobic protein SH are deleted. The genes are replaced by a chimeric gene encoding a heterologous entry protein derived from Vesicular Stomatitis Virus G protein or GP64 of baculovirus. These recombinant RSVs could be used as vaccine candidates (see D1, p.5, l.15 - p.8, l.20, p.14, l.17 - p.29, l.17).
Thus, the above document is novelty-destroying for the subject-matter of claims 1-8, 13-16 and 18.

2.2 D2 investigated the role of the attachment G glycoprotein of human RSV in viral infection. Mutant recombinant RSVs were constructed that do not express G (ΔG).

These recombinant viruses were recovered from the various mutant antigenomic cDNAs by cotransfection with N, P, M2-1, and L support plasmids and coinfection with MVA-T7 vaccinia virus (see D2, p.283, 'Abstract', p.284-294, 'Results' and 'Discussion').
Thus, the above document is novelty-destroying for the subject-matter of claims 1-14.

2.3 D3 describes the exploration of the roles of the G, F, and SH proteins in virion assembly, function, and cytopathology. For this reason full-length RSV cDNA has been modified and used to rescue infectious RSV lacking the G and/or SH genes. In order to rescue virus from the cDNA clones, the recombinant antigenomic plasmids have been cotransfected into Hep-2 cells along with plasmids expressing the RSV N, P, L, and M2-1 genes from the T7 promoter. The cells were also infected with a modified vaccinia virus, MVA-T7, to provide T7 polymerase (see D3, p.6825, 'Abstract', p.6826-6833, 'Materials and Methods, 'Results' and 'Discussion').
Thus, the above document is novelty-destroying for the subject-matter of claims 1-14.

2.4 The applicant is informed that due to the unclear and broad wording of the claims the teachings of the documents cited above will fall under the scope of the claims. The claims as they stand are definitely not restricted only to the use of homologous G or F or other essential proteins that are deleted and completed in *trans*, and also the scope of the claims is not restricted only to yield a pneumovirus that is neither underattenuated nor overattenuated.

3. The closest prior art to evaluate the inventiveness of claims 17 and 19 is also D1.
With respect to the subject-matter of the dependent claims 17 and 19 it is stated that these dependent claims do not appear to contain any additional features which, in combination with the features of any claim to which they refer, involve an inventive step, i.e. when taking the disclosure of D4 into account, referring to intranasal administration of *cp-52* RSV vaccine in adults, children and infants.

4. With respect to claims 18 and 19 you are already informed that in case of an European application said claims are not allowable because, "methods of treatment of the human or animal body by surgery or therapy and diagnostic methods practised

on the human or animal body shall not be regarded as inventions which are susceptible of industrial application."